

## **REMARKS**

Claims 1-14 were previously pending. Claim 3 has been amended for editorial purposes to deal with insufficient antecedent basis without narrowing the scope of the claim. The amendments to claim 1 are supported at least by the disclosures in page 4, lines 27-30 of the specification. New claim 15 has been added. This claim is supported at least by the disclosures in page 5, line 29 to page 16, line 11 of the specification. Applicants respectfully submit that no new matters have been introduced. Claims 1-15 will be pending upon entry of these amendments.

The specification has been amended to correct typographical errors in paragraphs [0005], [0007], [0024], [0033], [0044], and [0059] in the published application, US 2006-0121585 A1. Applicants note that these errors are present only in the published application, but not in the specification submitted by applicants on March 14, 2005. See page 3, line 20; page 4, line 20; page 9, line 24; page 12, line 26; page 16, line 10; page 20, line 9, of the specification filed.

Page 2, lines 19 and 20 of the specification as filed has been amended to correct some translation errors in the statement "copolyester containing, as a component, a hydroxyalkanoic acid other than 3HB and 3HV ...". By reading paragraph [0004] in its entirety, one skilled in the art would realize that the statement should be "copolyester containing, as components, 3HB and a hydroxyalkanoic acid other than 3HV ...". Poirier (BIO/TECHNOLOGY, 13, 142-150, 1995) cited in page 2, lines 28-29, of the specification discloses that hydroxyalkanoic acids other than 3HV, such as 3-hydroxypropionic acid ("3HP"), 3-hydroxyhexanoic acid ("3HH"), 3-hydroxyoctanoic acid ("3HO"), produced in bacteria may be incorporated into polyhydroxyalkanoates (PHAs). See Fig. 1; page 143, column 2, second full paragraph. Furthermore, the remaining part of paragraph [0004] of the instant application discusses copolymers containing 3HB and a hydroxyalkanoic acid other than 3HV, such as 3HH. Thus, one of ordinary skill would understand that in the clause "copolyester containing, as components, a hydroxyalkanoic acid other than 3HB

and 3HV”, the applicants intend to state “copolyester containing, as components, 3HB and a hydroxyalkanoic acid other than 3HV.”

### **References in Information Disclosure Statement**

The Examiner stated that two references, JP 57-150393 and JP 11-500008, in the Information Disclosure Statement submitted by applicants on June 13, 2005 were not provided and thus not considered. Applicants note that these two references, along with the English abstracts, were submitted on June 13, 2005 and can be found in the Patent Application Information Retrieval (PAIR) system in the USPTO website. To advance prosecution, copies of the two references, along with the English abstracts, are enclosed. Applicants request that the Examiner acknowledge that the two references are considered.

### **Specification**

The specification has been amended to correct typographical errors in paragraphs [0005], [0007], [0024], [0033], [0044], and [0059] in the published application. Applicants note that these errors are present only in the published application, U.S. 2006-0121585 A1, but not in the specification submitted by applicants on March 14, 2005. See page 3, line 20; page 4, line 20; page 9, line 24; page 12, line 26; page 16, line 10; page 20, line 9. If the Examiner considers that there are other typographical errors in the specification, applicants respectfully request that the Examiner point out specific locations of such errors.

### **Objections to Claim 1**

Claim 1 has been amended according to the Examiner’s suggestion.

### **Claim Rejection under 35 U.S.C. 112, Second Paragraph**

Claim 3 has been amended to recite “a composition,” “selecting the species,” and “a control value.” Applicants submit that claim 3 is now in

compliance with 35 U.S.C. 112, second paragraph. Withdrawal of the rejection is respectfully requested.

### **Claim Rejections under 35 U.S.C. 112, First Paragraph**

Applicants respectfully traverse the rejections of claims 1 and 3-8 under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants also respectfully traverse the rejections of claims 1 and 3-8 under 35 U.S.C. 112, first paragraph, as allegedly failing to enable production of 1) any copolyester, 2) using any microorganism, 3) using as a carbon source any oil and fat, and 4) any constant value of a specific substrate feed rate.

The Office Action contends at pages 4-5 that polyesters are “an extremely large and versatile family of the chemical compounds, therefore P(HB-co-3HH) species does not identify the genus as a whole.” Applicants point out that the written description of an application is not limited to the specific examples. In the present application, although P(HB-co-3HH) is described as an example, “there is no particular limitation on a copolyester capable of being applied to the culture method of the present invention, as long as it is a copolyester that may be obtained by polymerization of at least two monomeric units.” Page 5, lines 29-32. The amended claim 1 has been amended to limit the claimed polyester to be a biodegradable copolyester. New claim 15 recites: “The method of producing copolyester according to claim 1, wherein said copolyester comprises hydroxybutyric acid.” The instant specification describes, in an enabling way, methods of producing biodegradable copolyesters in a microorganism culture by controlling a specific substrate feed rate of an oil or fat to be used as a carbon source at a constant value throughout the whole culture period. An ordinary skilled in the art would understand that the claimed inventions can be carried out to produce any biodegradable copolyester, including a polyester comprising 3HB, without undue experimentation.

Based on the ground that the present application showed in Examples only the production of P(3B-co-3HH) by *Alcaligenes eutrophus* AC 32, the Office Action alleges that other microorganisms recited in claim 6 are not necessarily a suitable producers of P(3B-co-3HH). However, the present inventions can be performed not only to produce P(3B-co-3HH), but also to produce any biodegradable copolyesters that can be produced by microorganisms. Because the polyester in claim 1 is limited to a biodegradable copolyester, and the microorganism limited to a microorganism capable of producing a biodegradable copolyester, an ordinary skilled in the art would know which microorganisms to be used in the claimed process. Also, an ordinary skilled in the art would be able to perform the claimed inventions with any microorganism capable of producing a biodegradable copolyester without undue experimentation.

In the claimed inventions, any oil or fat can be used as the carbon source. An ordinary skilled in the art would understand that the oils and fats are converted to 3-hydroxyalkanoic acid monomer by  $\beta$ -oxidation. In the claimed methods, the incorporation rate of acyl-CoA to the polyester by  $\beta$ -oxidation depends on the feeding speed of oils and fats, providing a mechanism of controlling the composition ratios of monomers in the polyesters produced. For example, in page 23, Example 3 and Table 4, the 3HH composition ratio was successfully controlled by varying the feeding speeds of six different oils and fats. Thus, oils and fats should not be limited to the specific examples described in the application.

The Office Action states in page 5 that based on Figs. 1 and 2, "the constant value of the specific feed rate of the carbon source took place only during 36-70 h of culture," and thus "the limitation of claim 1 'a constant value [of the specific substrate feed rate] throughout the whole culture period' is not describing what applicants did." Applicants respectfully point out that the Office Action's conclusion is based on a misunderstanding of the definition of the specific substrate feed rate in the present application. **The specific substrate feed rate** is an amount of an oil or fat supplied **per net weight of cells** during a

unit time, or a **feed rate** of an oil or fat **per net weight of cells**. See page 10, lines 32-35; page 11, lines 5-9. When **the specific substrate feed rate** is kept constant, the feed rate of an oil or fat can change in proportion to a change in the net weight of the cells. Fig. 1 shows that the net weight of cells increased with time from 0 to about 36 hours of culture and then remained constant during 36-70 hours. Accordingly, the **feed rate** of oils and fats in Fig. 2 increased with time from 0 to about 36 hours of culture and then remained constant during 36-70 hours. From Figs. 1 and 2, we can see that the specific substrate feed rate, or the **feed rate** of oils and fats **per net weight of cells**, was kept constant throughout the whole culture period. Thus, the limitation in claim 1 “a constant value [of the specific substrate feed rate] throughout the whole culture period” has written description support in the specification. In addition, one of the key features of the claim inventions is that the yield of a copolymer or molar ratio of a monomer unit (e.g. 3HH) can be controlled by changing the specific substrate feed rate. See page 23, Example 3 and Table 4. As long as the specific substrate feed rate is constant throughout the culture period, the particular value of the specific substrate feed rate should not be limited.

For at least the foregoing reasons, claims 1 and 3-8 are fully in compliance with the written description and enablement requirements under 35 U.S.C. §112, first paragraph. Withdrawal of the rejections is respectfully requested.

#### Claim Rejections under 35 U.S.C. 102

Applicants respectfully traverse the rejections of claims 1, 3-4, and 6-8 under 35 U.S.C. 102(a) as being allegedly anticipated by JP 2001340078.

JP 2001340078 discloses a method of producing a polyester wherein the fatty acid is added continuously or in divided amounts to maintain the concentration of carbon source in order to avoid growth inhibition. See paragraph [0027]. For example, oils and fats were added continuously in Example 2 at a constant speed of 10 ml/min during 24-60 hours of the culture period. In Example 3, three equally divided portions of oils and fats were added

at 24, 36, and 48 hours after the start of the culture. in JP 2001340078, the feed rate, or the amount of oils and fats added per unit time, was not adjusted according to the net weight of the cells. Indeed, JP 2001340078 did not discuss the net weight of the cells at all.

Unlike JP 2001340078, the claimed inventions control the specific substrate feed rate, or the feed rate per net weight of the cells, at a constant value throughout the culture period. Applicants have discovered, surprisingly, that a constant specific substrate feed rate throughout the culture period resulted in a significant increase in the yield of copolymer polyesters. See page 13, lines 21-27. In addition, the molar ratio of 3HH in the copolymer increases when the specific substrate feed rate is kept at a low value. See Table 2; page 21, lines 29-35; page 14, line 33 to page 15, line 3. To the contrary, JP 2001340078, fails to teach or suggest a method of producing a polyester wherein the specific substrate feed rate is kept constant throughout the culture period. In Example 2 of JP 2001340078, the feed rate, or the amount of oils and fats added per unit time, was kept constant during 24-60 hours of the culture period. In Example 3, even the feed rate was not kept constant. JP 2001340078 does not disclose, explicitly or implicitly, controlling a specific substrate feed rate at a constant value throughout the culture period by adjusting the feed rate based on the net weight of the cells.

For at least the forgoing reasons, claims 1, 3-4, and 6-8 are not anticipated by JP 2001340078. Withdrawal of the rejections under 35 U.S.C. 102 is respectfully requested.

#### Claim Rejection under 35 U.S.C. 103

Applicants respectfully traverse the obviousness rejection of claim 5 under 35 U.S.C. 103(a) over JP 2001340078, alone and further in view of Chen G.Q. et al., *App. Microbio. Biotech.* 57: 50-55.

As discussed above, JP 2001340078 does not teach or suggest a method of producing a polyester wherein the specific substrate feed rate is kept constant throughout the culture period, as recited in present claim 1. The

deficiencies of JP 2001340078 are not cured by Chen G.Q. et al. Because JP 2001340078 and Chen G.Q., even when in combination, fail to teach or suggest each and every limitation of claim 1 (and claim 5 that depends on claim 1), a *prima facie* case of obviousness has not been established. Withdrawal of the rejection under 35 U.S.C. 103 is respectfully requested.

## CONCLUSION

The Examiner is encouraged to contact the undersigned regarding any questions concerning this amendment. In the event that the filing of this paper is deemed not timely, applicants petition for an appropriate extension of time. The Commissioner is authorized to debit Deposit Account No. 11-0600 the petition fee and any other fees that may be required in relation to this paper.

Respectfully submitted,  
KENYON & KENYON LLP

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By: King L. Wong  
King L. Wong  
Reg. No. 37,500

1500 K Street, N.W., Suite 700  
Washington, D.C. 20005-1257  
(202) 220-4200 (telephone)  
(202) 220-4201 (facsimile)

Enclosures:

JP 57-150393 and its English abstract  
JP 11-500008 and its English abstract